CLAIMS

1. Polypeptide, which has a binding affinity for HER2 and which is related to a domain of staphylococcal protein A (SPA) in that the sequence of the polypeptide corresponds to the sequence of the SPA domain having from 1 to about 20 substitution mutations.

2. Polypeptide according to claim 1, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-6} M.

3. Polypeptide according to claim 2, which has a binding affinity for HER2 such that the K_D value of the interaction is at most 1×10^{-7} M.

4. Polypeptide according to any one of claims 1-3, the sequence of which corresponds to the sequence of SPA protein Z, as set forth in SEQ ID NO:1, comprising from 1 to about 20 substitution mutations.

5. Polypeptide according to claim 4, comprising from 4 to about 20 substitution mutations.

6. Polypeptide according to claim 4 or 5, comprising substitution mutations at one or more of the positions 13, 14, 28, 32 and 35.

7. Polypeptide according to claim 6, additionally comprising substitution mutations at one or more of the positions 9, 10, 11, 17, 18, 24, 25 and 27.

8. Polypeptide according to any one of claims 4-7, comprising a substitution mutation at position 13 from phenylalanine to tyrosine.

9. Polypeptide according to any one of claims 4-8, comprising a substitution mutation at position 14 from tyrosine to tryptophan.

10. Polypeptide according to any one of claims 4-9, comprising a substitution mutation at position 28 from asparagine to an amino acid residue selected from arginine and histidine.

11. Polypeptide according to any one of claims 4-10, comprising a substitution mutation at position 28 from asparagine to arginine.

12. Polypeptide according to any one of claims 4-11, comprising a substitution mutation at position 32 from glutamine to arginine.

13. Polypeptide according to any one of claims 4-12, comprising a substitution mutation at position 35 from lysine to tyrosine.

14. Polypeptide according to any one of claims 4-13, comprising a substitution mutation at position 10 from glutamine to arginine.

15. Polypeptide according to any one of claims 4-14, comprising a substitution mutation at position 11 from asparagine to threonine.

16. Polypeptide according to any one of claims 4-15, comprising a substitution mutation at position 17 from leucine to valine.

17. Polypeptide according to any one of claims 4-12, comprising a substitution mutation at position 27 from arginine to an amino acid residue selected from lysine and serine.

18. Polypeptide according to any one of claims 4-17, the amino acid sequence of corresponds to that of SEQ ID NO:1, comprising at least the following mutations: F13Y, Y14W, N28R, Q32R and K35Y.

19. Polypeptide according to any one of claims 4-18, the amino acid sequence of which is as set out in any one of SEQ ID NO:2-79.

20. Polypeptide according to claim 19, the amino acid sequence of which is as set out in any one of SEQ ID NO:2-3.

21. Polypeptide according to any preceding claim, in which at least one of the asparagine residues present in the domain of staphylococcal protein A (SPA) to which said polypeptide is related has been replaced with another amino acid residue.

22. Polypeptide according to claim 21, the sequence of said domain of staphylococcal protein A (SPA) corresponding to the sequence of SPA protein Z as set forth in SEQ ID NO:1, and the polypeptide comprising substitution mutations at at least one position chosen from N3, N6, N11, N21, N23, N28, N43 and N52.

23. Polypeptide according to claim 22, comprising at least one of the following mutations: N3A, N6A, N6D, N11S, N23T, N28A and N43E.

24. Polypeptide, which constitutes a fragment of a polypeptide according to any preceding claim, which fragment retains binding affinity for HER2.

25. Polypeptide according to any preceding claim, which comprises additional amino acid residues at either terminal.

26. Polypeptide according to claim 25, in which the additional amino acid residues comprise a cysteine residue at the N- or C-terminal of the polypeptide.

27. Polypeptide according to any one of claims 25-26, in which the additional amino acid residues comprise a tag, preferably chosen from a hexahistidinyl tag, a myc tag and a flag tag.

28. Polypeptide according to any one of claims 25-26, in which the additional amino acid residues comprise at least one functional polypeptide domain, so that the polypeptide is a fusion polypeptide between a first moiety, consisting of the polypeptide according to any one of claims 1-24, and at least one second and optionally further moiety or moieties.

29. Polypeptide according to claim 28, in which the second moiety consists of one or more polypeptide(s) according to any one of claims 1-24, making the polypeptide a multimer of HER2 binding polypeptides according to any one of claims 1-24, the sequences of which may be the same or different.

30. Polypeptide according to claim 28, in which the second moiety comprises at least one polypeptide domain capable of binding to a target molecule other than HER2.

31. Polypeptide according to claim 30, in which the second moiety comprises at least one polypeptide domain capable of binding to human serum albumin.

32. Polypeptide according to claim 31, in which the at least one polypeptide domain capable of binding to human serum albumin is the albumin binding domain of streptococcal protein G.

33. Polypeptide according claim 30, in which the second moiety comprises a polypeptide which is related to a domain of staphylococcal protein A (SPA) in that the sequence of the polypeptide corresponds to the sequence of the SPA domain having from 1 to about 20 substitution mutations.

34. Polypeptide according claim 33, in which the sequence of the second moiety polypeptide corresponds to the sequence of SPA protein Z, as set forth in SEQ ID NO:1, having from 1 to about 20 substitution mutations.

35. Polypeptide according to claim 28, in which the second moiety is capable of enzymatic action.

36. Polypeptide according to claim 28, in which the second moiety is capable of fluorescent action.

37. Polypeptide according to claim 28, in which the second moiety is a phage coat protein or a fragment thereof.

38. Polypeptide according to any preceding claim, which comprises a label group.

39. Polypeptide according to claim 38, in which the label group is chosen from fluorescent labels, biotin and radioactive labels.

40. Polypeptide according to any one of the preceding claims, coupled to a substance having an activity against cells overexpressing HER2.

41. Polypeptide according to claim 40, in which said substance having an activity against cells overexpressing HER2 is chosen from cytotoxic agents, radioactive agents, enzymes for ADEPT applications, cytokines and procoagulant factors.

42. Nucleic acid molecule comprising a sequence encoding a polypeptide according to any one of claims 1-37.

43. Expression vector comprising the nucleic acid molecule according to claim 42.

44. Host cell comprising the expression vector according to claim 43.

45. Use of a polypeptide according to any one of claims 1-41 as a medicament.

46. Use of a polypeptide according to any one of claims 1-41 in the preparation of a medicament for the treatment of at least one form of cancer characterized by overexpression of HER2.

47. Method of treatment of at least one form of cancer characterized by overexpression of HER2, which method comprises administering to a subject in need of such treatment a therapeutically effective amount of a composition, which comprises a polypeptide according to any one of claims 1-41 as an active substance.

48. Use of a polypeptide according to any one of claims 1-41 conjugated to a substance with anti-cancer activity for delivery of said substance to cells that overexpress HER2.

49. Method of directing a substance having an anti-cancer activity to cells overexpressing HER2 *in vivo*, which method comprises administering a conjugate of said substance and a polypeptide according to any one of claims 1-41 to a subject.

50. Use of a polypeptide according to any one of claims 1-41 for the detection of HER2 in a sample.

51. Method of detection of HER2 in a sample, in which method a polypeptide according to any one of claims 1-41 is used.

52. Method according to claim 51, comprising the steps: (i) providing a sample to be tested, (ii) applying a polypeptide according to any one of claims 1-41 to the sample under conditions such that binding of the polypeptide to any HER2 present in the sample is enabled, (iii) removing non-bound polypeptide, and (iv) detecting bound polypeptide.

53. Method according to claim 52, in which the sample is a biological fluid sample, preferably a human blood plasma sample.

54. Method according to claim 52, in which the sample is a tissue sample, preferably a human tissue sample, more preferably a biopsy sample from a human suffering from cancer.

55. Kit for diagnosis of HER2 overexpression in a tissue sample, which kit comprises a polypeptide according to any one of claims 1-41 fused to a reporter enzyme, reagents for detection of activity of said reporter enzyme, and positive and negative control tissue slides.

56. Kit for *in vivo* diagnosis of HER2 overexpression, which kit comprises a polypeptide according to any one of claims 1-41 labeled with a chelator, a diagnostic radioactive isotope, and reagents for the analysis of the incorporation efficiency.

57. Kit for performing the method of claim 49, which kit comprises a polypeptide according to any one of claims 1-41 labeled with a chelator, a therapeutic radioactive isotope, and reagents for the analysis of the incorporation efficiency.